

What is claimed is:

Sub E1 1. A pharmaceutical composition comprising a nucleic acid and a penetration enhancer.

Sub B1 2. ~~The pharmaceutical composition of claim 1, wherein~~
5 said nucleic acid is an oligonucleotide or a bioequivalent thereof and said penetration enhancer is a surfactant, a fatty acid, a bile salt, a chelating agent or a non-chelating non-surfactant.

3. ~~The pharmaceutical composition of claim 1, wherein~~
10 ~~said nucleic acid is an oligonucleotide in prodrug form or a~~
~~bioequivalent thereof.~~

4. ~~The pharmaceutical composition of claim 1, wherein~~
said penetration enhancer is ~~a~~ fatty acid.

Sub E3 5. ~~The pharmaceutical composition of claim 4, wherein~~
15 said fatty acid is arachidonic acid, oleic acid, lauric acid, caprylic acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein, dilaurin, glyceryl 1-monocaprate, 1-dodecylazacycloheptan-2-one, an acylcarnitine, an acylcholine, 20 or a monoglyceride, a diglyceride or a pharmaceutically acceptable salt ~~thereof~~.

6. ~~The pharmaceutical composition of claim 1, wherein~~
said penetration enhancer is a bile salt.

7. ~~The pharmaceutical composition of claim 1, wherein~~
25 said penetration enhancer is cholic acid, dehydrocholic acid, deoxycholic acid, ~~gluc~~cholic acid, glycholic acid, glycodeoxycholic acid, taurocholic acid, taurodeoxycholic acid, chenodeoxycholic acid, ursodeoxycholic acid, sodium tauro-24,25-dihydro-fusidate, sodium glycodihydrofusidate, 30 polyoxyethylene-9-lauryl ether or a pharmaceutically acceptable

salt thereof.

8. The pharmaceutical composition of claim 1, wherein said penetration enhancer is a chelating agent, a surfactant penetration enhancer or a non-chelating non-surfactant 5 penetration enhancer.

9. The pharmaceutical composition of claim 1, wherein said penetration enhancer is EDTA, citric acid, a salicylate, a *N*-acyl derivative of collagen, laureth-9, an *N*-amino acyl derivative of a beta-diketone or a mixture thereof.

10 10. The pharmaceutical composition of claim 1, wherein said penetration enhancer is sodium lauryl sulfate, polyoxyethylene-9-lauryl ether, polyoxyethylene-20-cetyl ether, a perfluorchemical emulsion or a mixture thereof.

11. The pharmaceutical composition of claim 1, wherein 15 said penetration enhancer is an unsaturated cyclic urea, a 1-alkyl-alkanone, a 1-alkenylazacyclo-alakanone, a steroidal anti-inflammatory agent or a mixture thereof.

12. The pharmaceutical composition of claim 1, further comprising at least one carrier compound.

20 13. The pharmaceutical composition of claim 12, wherein said carrier compound is selected from the group consisting of polyinosinic acid, dextran sulfate, polycytidic acid and 4-acetamido-4'isothiocyanostilbene-2,2'-disulfonic acid.

14. The pharmaceutical composition of claim 2 further 25 comprising an additional penetration enhancer.

15. The pharmaceutical composition of claim 14, wherein said penetration enhancer is a fatty acid and said additional penetration enhancer is a surfactant, a bile salt, a chelating agent or a non-chelating non-surfactant.

16. The pharmaceutical composition of claim 14, wherein said penetration enhancer is a surfactant and said additional penetration enhancer is a fatty acid, a bile salt, a chelating agent or a non-chelating non-surfactant.

5 17. The pharmaceutical composition of claim 14, wherein said penetration enhancer is a bile salt and said additional penetration enhancer is a fatty acid, a surfactant, a chelating agent or a non-chelating non-surfactant.

10 18. The pharmaceutical composition of claim 14, wherein said penetration enhancer is a chelating agent and said additional penetration enhancer is a bile salt, a fatty acid, a surfactant or a non-chelating non-surfactant.

15 19. The pharmaceutical composition of claim 14, wherein said penetration enhancer is a non-chelating non-surfactant and said additional penetration enhancer is a bile salt, a fatty acid, a surfactant or a chelating agent.

20 20. A pharmaceutical composition comprising a nucleic acid and three or more penetration enhancers.

20 21. The pharmaceutical composition of claim 14, further comprising one or more carrier compounds.

20 22. The pharmaceutical composition of claim 20, further comprising one or more carrier compounds.

20 23. The pharmaceutical composition of claim 2, wherein said oligonucleotide is an antisense oligonucleotide.

25 24. The pharmaceutical composition of claim 23, wherein said antisense oligonucleotide modulates the expression of a cellular adhesion protein or the rate of cellular proliferation, or has biological activity against miscellaneous disorders, diseases resulting from eukaryotic pathogens, 30 retroviruses including HIV or non-retroviral viruses.

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Sub
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25. A method of treating an animal having or suspected of having a disease or disorder that is treatable in whole or in part with one or more nucleic acids comprising administering to said animal a therapeutically effective amount of the 5 pharmaceutical composition of claim 1.

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E4*
26. The method of claim 23, wherein said administration is sublingual, endoscopic or rectal.

27. The method of claim 23, wherein said administration is oral.

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Y3*
10 28. A method of investigating the role of gene or gene product in an animal other than a human comprising administering to said animal a biologically active amount of the pharmaceutical composition of claim 1.

29. The method of claim 28, wherein said administration 15 is sublingual, endoscopic or rectal.

30. The method of claim 28, wherein said administration is oral.

31. The pharmaceutical composition of claim 2 wherein said surfactant is Tween 80.

20 32. The pharmaceutical composition of claim 3 wherein said oligonucleotide has at least one chemical modification selected from the group consisting of a modified nucleobase, a modified sugar residue, or a modified backbone linkage.

25 33. The pharmaceutical composition of claim 3 wherein said oligonucleotide has at least one chemical modification selected from the group consisting of a cytosine to 5-methyl-cytosine substitution, a phosphorothioate linkage and a 2'-methoxyethoxy modification.

34. The pharmaceutical composition of claim 6, wherein said bile salt is present in its acid form, as a sodium salt, or in a mixture of said acid form and said sodium salt.

35. The pharmaceutical composition of claim 1 wherein 5 said pharmaceutical composition is water based.

36. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition is propylene glycol based.

37. The pharmaceutical composition of claim 1 wherein 10 said pharmaceutical composition comprises less than about 8% water.

38. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition, when administered to a mammal, results in more than about 15% bioavailability of said nucleic acid in said mammal.

15 39. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition, when administered to a mammal, results in from about 17% to about 35% bioavailability of said nucleic acid in said mammal.

40. A method of modulating gene expression in cells, 20 tissues or organisms comprising administering the pharmaceutical composition of claim 1 to said cells, tissues or organisms.

add E6

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